REMARKS/ARGUMENTS

Examiner Interview

Applicants thank Examiner Sullivan for the courtesy extended to their representative, Melissa E. Kolom, during the telephonic interview held on December 22, 2006. The matters discussed during the interview are substantially as set forth herein.

The Pending Claims

Claims 36, 37, 40-70, 73, and 74 are pending. Claims 36, 37, and 40-50 are directed to a bacterial artificial chromosome (BAC). Claims 51-56 are directed to a cell comprising the BAC, and claims 57-66 are directed to a method of producing the BAC. Claims 67-70 are directed to a method of mutagenizing an infectious herpes viral genomic sequence in the aforementioned BAC. Claims 73 and 74 are directed to an isolated or purified infectious herpes virus genomic sequence produced by the aforementioned method of mutagenizing an infectious herpes viral genomic sequence.

The Office Action

The Office Action maintains that the pending claims are not entitled to the benefit of foreign priority because the German application to which the subject application claims priority is not enabled. As a result, the Office Action maintains the rejections of the claims under 35 U.S.C. §§ 102(a) and 102(e) in view of the Messerle 1997 reference, the Delecluse reference, or the '621 patent. The Office Action also rejects claims 73 and 74 under 35 U.S.C. § 102(b) as allegedly anticipated by Messerle et al., *J. Mol. Med.*, *74*, Abstract No. 4, p. B8 (1996) ("the Messerle 1996 reference"). Reconsideration of these rejections is respectfully requested.

Discussion of Priority

According to the Office Action, the pending claims are not entitled to the benefit of foreign priority under 35 U.S.C. § 119 because the German patent application to which the present application claims priority ("the German priority application") is non-enabling. In particular, the Office Action alleges that the German priority application is not enabling because it discloses that the use of BACs comprising bacterial sequences other than low-copy

vectors was unpredictable at the time the German priority application was filed. In support of this allegation, the Office Action points to the teaching in the German priority application that "suitable cloning vehicles are low-copy vectors, since the stability of the cloned DNA is only ensured by the low number of copies of the plasmids" (see English translation of German priority application at page 4, lines 1-3). As further evidence of the alleged unpredictability associated with using the claimed BAC vectors, the Office Action relies on Warnes et al., *Plasmid, 16*: 116-123 (1986), which allegedly teaches that plasmids containing large inserts (i.e., 21 kb) of CMV genomic DNA are unstable when grown in eukaryotic cells.

Long before the filing of the present application and the German priority application, a BAC was well known in the art as a cloning vector based on the *E. coli* F plasmid, which can accept large DNA inserts (e.g., 100-300 kB) and is maintained in low copy number (1-2 copies per cell). For example, Shizuya et al., *Proc. Natl. Acad. Sci. USA, 89*: 8794-8797 (1992) ("the Shizuya reference," enclosed herewith), discloses one of the first uses of a BAC to clone large sequences of human DNA. The BAC vector disclosed in the Shizuya reference is called pBAC108L, and is based on the mini-F plasmid pMBO131 of *E. coli* (Shizuya reference at page 8794, right column, first complete paragraph, and Figure 1). Thus, contrary to the allegation of the Office Action, making and using BACs to clone large DNA inserts was not unpredictable at the time the German priority application was filed and could be accomplished by one of ordinary skill in the art without undue experimentation.

During the Examiner interview, Examiner Sullivan expressed doubt as to whether the BACs disclosed in both the German priority application and the present application were similar to the BACs previously described in the prior art (such as the Shizuya reference), and whether such BACs could be maintained at low copy number in host cells. Applicants note that both the German priority application and the present application disclose that the presently claimed BAC vector is derived from an *E. coli* mini-F plasmid (see English translation of German priority application and present application at pages 3 and 4, bridging paragraph). In fact, the Examples of both the German priority application and the present application disclose a method of constructing a BAC vector (pKSO) based on plasmid pBAC108L disclosed in the Shizuya reference (see German priority application at page 7, lines 25-32, and page 14, reference no. 19, and present application at page 15, lines 2-7, and page 36, reference no. 19).

Therefore, based on the knowledge in art at the time the German priority application was filed, coupled with the guidance provided by both the German priority application and the present application, there is no doubt that the claimed BAC vectors are maintained at low copy number, are stable, and can accept and propagate large DNA inserts (e.g., 100-300 kB). Accordingly, the subject matter of the pending claims clearly comports with, and is enabled by, the disclosures of the German priority application and the present application. As such, Applicants request that the pending claims be accorded the benefit of the German priority application under 35 U.S.C. § 119.

Discussion of Rejections Under 35 U.S.C. §§ 102(a) and (e)

Claims 36, 37, 40-43, 45-52, 53-64, and 67-70 are rejected under Section 102(a) as allegedly anticipated by the Messerle 1997 reference. Claims 36, 43, 48, 51, 54, 57-60, and 63 are rejected under Section 102(a) as allegedly anticipated by the Delecluse reference. Claims 37 and 40-43 are rejected under Section 102(e) as allegedly anticipated by the '621 patent.

A publication qualifies as prior art under Section 102(a) if the publication was by another and occurred prior to the date of invention for the claims in issue. A patent qualifies as prior art under Section 102(e) if the patent has an effective U.S. filing date prior to the date of invention for the claims in issue. Here, the Messerle 1997 reference was published in December 1997, and the Delecluse reference was published in July 1998. The '621 patent allegedly has an effective U.S. filing date of February 26, 1998. However, the date of invention for the claims in issue is at least as early as August 1, 1997, i.e., before the publication dates of the Messerle 1997 reference and the Delecluse reference, and before the alleged effective U.S. filing date of the '621 patent, as previously demonstrated by the text of the German patent application to which the present application claims priority under 35 U.S.C. § 119.

As a result, the Messerle 1997 reference and the Delecluse reference are not prior art to the pending claims under 35 U.S.C. § 102(a), and the '621 patent is not prior art to the pending claims under 35 U.S.C. § 102(e). See also M.P.E.P. § 2136.05.

Discussion of Rejections Under 35 U.S.C. § 102(b)

Claims 73 and 74 are rejected under Section 102(b) as allegedly anticipated by the Messerle 1996 reference.

Claim 73 is directed to an isolated or purified infectious herpes virus genomic sequence produced by the method of claim 67, wherein the infectious herpes virus genomic sequence comprises a mutagenized viral genomic sequence larger than 100 kb. Claim 67 requires introducing a BAC comprising an infectious herpes virus genomic sequence into a bacterial host cell, exposing the BAC to mutagenizing DNA molecules, and mutagenizing the infectious herpes virus genomic sequence in the BAC. In contrast, the Messerle 1996 reference discloses transfecting eukaryotic cells with two BAC/MCMV hybrid plasmids which do not contain infectious viral genomic sequences. In particular, the Messerle 1996 reference states "[t]ransfection of each plasmid alone into eukaryotic cells did not result in the production of a progeny." Thus, the two individual plasmids described by the Messerle 1996 reference do not contain an infectious herpes virus genomic sequence capable of being replicated and packaged in the viral host. Infectious viral progeny can only be obtained by co-transfection of both plasmids. Moreover, one of ordinary skill in the art following the teachings of the Messerle 1996 reference could not have isolated a homogenous plasmid preparation from the transfected cells. In this regard, the two plasmids disclosed in the Messerle 1996 reference recombine in the cell resulting in different recombination products. Isolating the recombined plasmid constructs from the cells would lead to a heterogeneous mixture of plasmids.

This is in distinct contrast to the present invention, which provides an isolated or purified infectious mutagenized herpes virus genomic sequence larger than 100 kb that is homogeneous and produced from a single BAC vector. Furthermore, the Messerle 1996 reference does not disclose exposing the BAC to mutagenizing DNA molecules.

Thus, the Messerle 1996 reference does not disclose the subject matter of claim 73, or claim 74 depending therefrom. Accordingly, the rejection under Section 102(b) should be withdrawn.

Discussion of Rejections Under 35 U.S.C. § 103

Claims 37 and 40-43 remain rejected under Section 103(a) as allegedly obvious over the '621 patent in view of the Messerle 1996 reference. As discussed above, the '621 patent is not prior art to the pending claims. Moreover, the Messerle 1996 reference does not disclose a (BAC) containing bacterial nucleic acid sequences and an infectious herpes virus genomic sequence larger than 200 kb, wherein the BAC enables replication of the infectious herpes virus genomic sequence in a host cell. Thus, the invention defined by claims 37 and 40-43 is not obvious in view of the cited references, whether considered alone or in combination. Applicants, therefore, respectfully request withdrawal of the Section 103 rejection.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,

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